

**In the claims:**

1. (Previously Presented) A method of reducing extracellular brain glutamate levels in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a glutamate modifying enzyme capable of reducing blood glutamate levels, thereby reducing extracellular brain glutamate levels.

2. (Currently Amended) The method of claim 1, wherein said glutamate modifying enzyme is a naturally occurring enzyme.

3. (Previously Presented) The method of claim 1, wherein said at least one glutamate modifying enzyme is selected from the group consisting of a transaminase, a dehydrogenase, a decarboxylase, a ligase, an aminomutase, a racemase and a transferase.

4. (Original) The method of claim 3, wherein said transaminase is selected from the group consisting of glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, acetylornithine transaminase, ornithine-oxo-acid transaminase, succinyldiaminopimelate transaminase, 4-aminobutyrate transaminase, (s)-3-amino-2-methylpropionate transaminase, 4-hydroxyglutamate transaminase, diiodotyrosine transaminase, thyroid-hormone transaminase, tryptophan transaminase, diamine transaminase, cysteine transaminase, L-Lysine 6-transaminase, histidine transaminase, 2-aminoadipate transaminase, glycine transaminase, branched-chain-amino-acid transaminase, 5-aminovalerate transaminase, dihydroxyphenylalanine transaminase, tyrosine transaminase, phosphoserine transaminase, taurine transaminase, aromatic-amino-acid transaminase, aromatic-amino-acid-glyoxylate transaminase, leucine transaminase, 2-aminohexanoate transaminase, ornithine(lysine) transaminase, kynurenine-oxoglutarate transaminase, D-4-hydroxyphenylglycine transaminase, cysteine-conjugate transaminase, 2,5-diaminovalerate transaminase, histidinolphosphate transaminase, diaminobutyrate-2-oxoglutarate transaminase, and udp-2-acetamido-4-amino-2,4,6-trideoxyglucose transaminase.

5-9. (Canceled)

10. (Previously Presented) The method of claim 1, further comprising administering to the subject at least one co-factor of a glutamate modifying enzyme.

11. (Original) The method of claim 10, wherein said co-factor is selected from the group consisting of oxaloacetate, pyruvate,  $\text{NAD}^+$ ,  $\text{NADP}^+$ , 2-oxohexanedioic acid, 2-oxo-3-sulfopropionate, 2-oxo-3-sulfinopropionic acid, 2-oxo-3-phenylpropionic acid, 3-indole-2-oxopropionic acid, 3-(4-hydroxyphenyl)-2-oxopropionic acid, 4-methylsulfonyl-2-oxobutyric acid, 3-hydroxy-2-oxopropionic acid, 5-oxopentanoate, 6-oxo-hexanoate, glyoxalate, 4-oxobutanoate,  $\alpha$ -ketoisocaproate,  $\alpha$ -ketoisovalerate,  $\alpha$ -keto- $\beta$ -methylvalerate, succinic semialdehyde-(4-oxobutyrate), pyridoxal phosphate, pyridoxal phosphate precursors and 3-oxoisobutanoate.

12. (Currently Amended) The method of claim 1, wherein said glutamate modifying enzyme is an artificially modified glutamate modifying enzyme incapable of converting a ~~modified~~ glutamate metabolite into glutamate.

13. (Previously Presented) The method of claim 12, wherein said artificially modified glutamate modifying enzyme is an artificially modified human GOT.

14. (Previously Presented) The method of claim 1, further comprising administering to the subject a co-factor of said glutamate modifying enzyme, said glutamate modifying enzyme being artificially modified glutamate modifying enzyme incapable of converting modified glutamate into glutamate.

15. (Previously Presented) The method of claim 14, wherein said co-factor is selected from the group consisting of lipoic acid, lipoic acid precursor, pyridoxal phosphate, pyridoxal phosphate precursor, thiamine pyrophosphate and thiamine pyrophosphate precursor.

16-25. (Canceled)

26. (Previously Presented) The method of claim 1, wherein said administering is effected at a concentration of said enzyme not exceeding 1 g/Kg body weight/hour.

27-119. (Canceled)

120. (Previously Presented) The method of claim 1, wherein said glutamate modifying enzyme is a glutamate oxaloacetate transaminase.

121. (Previously Presented) The method of claim 120, further comprising administering oxaloacetate.

122. (Previously Presented) A method of reducing extracellular brain glutamate levels, the method comprising administering to a subject in need thereof a therapeutically effective amount of a glutamate modifying enzyme and a co-factor thereof, thereby reducing extracellular brain glutamate levels.

123. (Previously Presented) The method of claim 122, wherein said glutamate modifying enzyme is glutamate oxaloacetate transaminase and said co-factor is oxaloacetate.

124. (Previously Presented) The method of claim 122, wherein said glutamate modifying enzyme is a naturally occurring enzyme.

125. (Currently Amended) The method of claim 122, wherein said glutamate modifying enzyme is an artificially modified glutamate modifying enzyme incapable of converting ~~modified-a~~ glutamate metabolite into glutamate.

126. (Previously Presented) A method of reducing extracellular brain glutamate levels, the method comprising administering to a subject in need thereof a pharmaceutical composition which comprises a therapeutically effective amount of a co-factor of a glutamate modifying enzyme with the proviso that when said co-factor is oxaloacetate said pharmaceutical composition does not comprise sugar, thereby reducing extracellular brain glutamate levels.

127. (Previously Presented) The method of claim 126, wherein said co-factor of said glutamate modifying enzyme is selected from the group consisting of oxaloacetate, pyruvate,  $\text{NAD}^+$ ,  $\text{NADP}^+$ , 2-oxohexanedioic acid, 2-oxo-3-sulfopropionate, 2-oxo-3-sulfinopropionic acid, 2-oxo-3-phenylpropionic acid, 3-indole-2-oxopropionic acid, 3-(4-hydroxyphenyl)-2-oxopropionic acid, 4-methylsulfonyl-2-oxobutyric acid, 3-hydroxy-2-oxopropionic acid, 5-oxopentanoate, 6-oxo-hexanoate, glyoxalate, 4-oxobutanoate,  $\alpha$ -ketoisocaproate,  $\alpha$ -ketoisovalerate,  $\alpha$ -keto- $\beta$ -methylvalerate, succinic semialdehyde-(-4-oxobutyrate), pyridoxal phosphate, pyridoxal phosphate precursors and 3-oxoisobutanoate.

128. (New) The method of claim 1, wherein said administering is effected to a peripheral blood of the subject.

129. (New) The method of claim 122, wherein said administering is effected to a peripheral blood of the subject.

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130. (New) The method of claim 126, wherein said administering is effected to a peripheral blood of the subject.